

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: :  
Bernd RIEDL et al. : Group Art Unit: TO BE ASSIGNED  
Serial No.: TO BE ASSIGNED : Examiner: TO BE ASSIGNED  
Filed: January 11, 2002 :  
For:  $\omega$ -CARBOXYARL SUBSTITUTED DIPHENYL UREAS AS RAF KINASE  
INHIBITORS

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Prior to the calculation of the fee for the examination of the accompanying application,  
please amend the claims as follows.

**IN THE SPECIFICATION**

Page 1, line 1, after the title insert

--Priority is claimed to provisional application Serial No. (Unassigned), filed on January  
12, 2001.--

**IN THE CLAIMS**

Please cancel claims 4, 5, 14, 16, 20, 23-26, 29-31, 34-36, 40-43, 51 and 55-65 without  
prejudice or disclaimer.

Please amend claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 44-50 and 52-54 as  
follows.

1. (Amended) A method for the treatment of cancerous cell growth mediated by RAF

kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-\text{NH}-\text{C}(\text{O})-\text{NH}-$ ,

A is a substituted moiety of up to 40 carbon atoms of the formula:  $-\text{L}-(\text{M}-\text{L}^1)_q$ , where L is a 5 or 6 membered cyclic structure bound directly to D,  $\text{L}^1$  comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and  $\text{L}^1$  contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein  $\text{L}^1$  is substituted by at least one substituent selected from the group consisting of  $-\text{SO}_2\text{R}_x$ ,  $-\text{C}(\text{O})\text{R}_x$  and  $-\text{C}(\text{NR}_y)\text{R}_z$ ,

$\text{R}_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

$\text{R}_x$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

$\text{R}_z$  is  $\text{R}_x$  or  $\text{NR}_a\text{R}_b$  where  $\text{R}_a$  and  $\text{R}_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms

selected from N, S and O and are optionally substituted by halogen, or

$-\text{OSi}(\text{R}_i)_3$ , where  $\text{R}_i$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $\text{R}_a$  and  $\text{R}_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $\text{R}_a$  or  $\text{R}_b$  is  $-\text{C}(\text{O})-$ , a  $\text{C}_1-\text{C}_5$  divalent alkylene group or a substituted  $\text{C}_1-\text{C}_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $\text{C}_1-\text{C}_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or  $\text{L}^1$  is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and  $\text{W}_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^7$ ,  $-\text{C}(\text{O})\text{NR}^7\text{R}^7$ ,  $-\text{C}(\text{O})-\text{R}^7$ ,  $-\text{NO}_2$ ,  $-\text{OR}^7$ ,  $-\text{SR}^7$ ,  $-\text{NR}^7\text{R}^7$ ,  $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$ ,  $-\text{NR}^7\text{C}(\text{O})\text{R}^7$ ,  $-\text{Q}-\text{Ar}$ , and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^7$ ,  $-\text{C}(\text{O})\text{R}^7$ ,  $-\text{C}(\text{O})\text{NR}^7\text{R}^7$ ,  $-\text{OR}^7$ ,  $-\text{SR}^7$ ,  $-\text{NR}^7\text{R}^7$ ,  $-\text{NO}_2$ ,  $-\text{NR}^7\text{C}(\text{O})\text{R}^7$ ,  $-\text{NR}^7\text{C}(\text{O})\text{OR}^7$  and halogen up to per-halo; with each  $\text{R}^7$  independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{N}(\text{R}^7)-$ ,  $-(\text{CH}_2)_m-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{CH}(\text{OH})-$ ,  $-(\text{CH}_2)_m\text{O}-$ ,  $-(\text{CH}_2)_m\text{S}-$ ,

$-(CH_2)_mN(R^7)-$ ,  $-O(CH_2)_m-CHX^a-$ ,  $-CX^a_{2^7}-$ ,  $-S-(CH_2)_m-$  and  $-N(R^7)(CH_2)_m-$ , where  $m=1-3$ , and  $X^a$  is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ , and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-COR^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NO_2$ ,  $-NR^7R^7$ ,  $-NR^7C(O)R^7$ , and  $-NR^7C(O)OR^7$ , with  $R^7$  as defined above.

## 2. (Amended) A method as in claim 1 wherein:

$R_y$  is hydrogen,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl having 0-3 heteroatoms,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkenoyl,  $C_{6-12}$  aryl,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O,  $C_{7-24}$  aralkyl,  $C_{7-24}$  alkaryl, substituted  $C_{1-10}$  alkyl, substituted  $C_{1-10}$  alkoxy, substituted  $C_{3-10}$  cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted  $C_6-C_{14}$  aryl, substituted  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O, substituted  $C_{7-24}$  alkaryl or substituted  $C_7-C_{24}$  aralkyl, where  $R_y$  is a substituted group, it is substituted by halogen up to per halo,

$R_z$  is hydrogen,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl having 0-3 heteroatom,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkenoyl,  $C_{6-12}$  aryl,  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from, S, N and O,  $C_{7-24}$  alkaryl,  $C_{7-24}$  aralkyl, substituted  $C_{1-10}$  alkyl, substituted  $C_{1-10}$  alkoxy, substituted  $C_6-C_{14}$  aryl, substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from S, N and O, substituted  $C_{7-24}$  alkaryl or substituted  $C_7-C_{24}$  aralkyl where  $R_z$  is a substituted group, it is substituted by halogen up to per halo, hydroxy,  $C_{1-10}$  alkyl,  $C_{3-12}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O,  $C_{1-10}$  alkoxy,  $C_{6-12}$  aryl,  $C_{1-6}$  halo substituted alkyl up to per halo alkyl,  $C_6-C_{12}$  halo substituted aryl up to per halo aryl,  $C_3-C_{12}$  halo

substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted C<sub>7</sub>-C<sub>24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7</sub>-C<sub>24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

R<sub>a</sub> and R<sub>b</sub> are,

a) independently hydrogen,

a carbon based moiety selected from te group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>2-10</sub> alkenyl, C<sub>1-10</sub> alkenoyl, C<sub>6-12</sub> aryl, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from O, N and S, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, C<sub>7-24</sub> aralkyl, C<sub>7</sub>-C<sub>24</sub> alkaryl, substituted C<sub>1-10</sub> alkyl, substituted C<sub>1-10</sub> alkoxy, substituted C<sub>3-10</sub> cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C<sub>6-12</sub> aryl, substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C<sub>7-24</sub> aralkyl, substituted C<sub>7-24</sub> alkaryl, where R<sub>a</sub> and R<sub>b</sub> are a substituted group, they are substituted by halogen up to per halo, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>1-6</sub> halo substituted alkyl up to per halo alkyl, C<sub>6</sub>-C<sub>12</sub> halo substituted aryl up to per halo aryl, C<sub>3</sub>-C<sub>12</sub> halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7</sub>-C<sub>24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7</sub>-C<sub>24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub> ; or

-OSi(R<sub>f</sub>)<sub>3</sub> where R<sub>f</sub> is hydrogen, C<sub>1-10</sub> alkyl, C<sub>1-10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>6-12</sub> aryl, C<sub>3</sub>-C<sub>12</sub> hetaryl having 1-3 heteroatoms selected from O, S and N, C<sub>7-24</sub> aralkyl, substituted C<sub>1-10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, substituted C<sub>3</sub>-C<sub>12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C<sub>3</sub>-C<sub>12</sub> heteraryl having 1-3 heteroatoms selected from O, S, and N, substituted C<sub>6-12</sub> aryl, and substituted C<sub>7-24</sub> alkaryl, where R<sub>f</sub> is a substituted group it is substituted halogen up to per halo, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub>

hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>7-C24</sub> alkaryl, C<sub>7-C24</sub> aralkyl, C<sub>1-6</sub> halo substituted alkyl up to per halo alkyl, C<sub>6-C12</sub> halo substituted aryl up to per halo aryl, C<sub>3-C12</sub> halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3-C12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7-C24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7-C24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>7-C24</sub> alkaryl, C<sub>7-C24</sub> aralkyl, halo substituted C<sub>1-6</sub> alkyl up to per halo alkyl, halo substituted C<sub>6-C12</sub> aryl up to per halo aryl, halo substituted C<sub>3-C12</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3-C12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7-C24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7-C24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

or

c) one of R<sub>a</sub> or R<sub>b</sub> is -C(O)-, a C<sub>1-C5</sub> divalent alkylene group or a substituted C<sub>1-C5</sub> divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C<sub>1-C5</sub> divalent alkylene group are selected from the group consisting of halogen, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>7-C24</sub> alkaryl, C<sub>7-C24</sub> aralkyl, C<sub>1-6</sub> halo substituted alkyl up to per halo alkyl, C<sub>6-C12</sub> halo substituted aryl up to per halo aryl, C<sub>3-C12</sub> halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3-C12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7-C24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7-C24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

where  $R_g$  is  $C_{1-10}$  alkyl,  $-CN$ ,  $-CO_2R_d$ ,  $-OR_d$ ,  $-SR_d$ ,  $-NO_2$ ,  $-C(O)R_e$ ,  $-NR_dR_e$ ,  $-NR_dC(O)OR_e$  and  $-NR_dC(O)R_e$ , and  $R_d$  and  $R_e$  are independently selected from the group consisting of hydrogen,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S,  $C_{6-12}$  aryl,  $C_3-C_{12}$  hetaryl with 1-3 heteroatoms selected from O, N and S and  $C_7-C_{24}$  aralkyl,  $C_7-C_{24}$  alkaryl, up to per halo substituted  $C_1-C_{10}$  alkyl, up to per halo substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted  $C_6-C_{14}$  aryl, up to per halo substituted  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted  $C_7-C_{24}$  alkaryl up to per halo alkaryl, and up to per halo substituted  $C_7-C_{24}$  aralkyl,

W is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-C(O)-R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ ;  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_2-C_{10}$  alkenyl,  $C_1-C_{10}$  alkenoyl,  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_6-C_{14}$  aryl,  $C_7-C_{24}$  alkaryl,  $C_7-C_{24}$  aralkyl,  $C_3-C_{12}$  heteroaryl having 1-3 heteroatoms selected from O, N and S,  $C_4-C_{23}$  alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted  $C_1-C_{10}$  alkyl, substituted  $C_1-C_{10}$  alkoxy, substituted  $C_2-C_{10}$  alkenyl, substituted  $C_1-C_{10}$  alkenoyl, substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted  $C_6-C_{12}$  aryl, substituted  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from O, N and S, substituted  $C_7-C_{24}$  aralkyl, substituted  $C_7-C_{24}$  alkaryl, substituted  $C_4-C_{23}$  alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and  $-Q-Ar$ ;

$R^7$  is independently selected from H,  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_2-C_{10}$  alkenyl,  $C_1-C_{10}$  alkenoyl,  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_6-C_{14}$  aryl,  $C_3-C_{13}$  hetaryl having 1-3 heteroatoms selected from O, N and S,  $C_7-C_{14}$  alkaryl,  $C_7-C_{24}$  aralkyl,  $C_4-C_{23}$  alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted  $C_1-C_{10}$  alkyl, up to per-halosubstituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per-halosubstituted  $C_6-C_{14}$  aryl, up to per-halosubstituted  $C_3-C_{13}$  hetaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted  $C_7-C_{24}$  aralkyl, up to per-

halosubstituted C<sub>7</sub>-C<sub>24</sub> alkaryl, and up to per-halosubstituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkenoyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, N and S, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> hetaryl having 1-3 heteroatoms selected from O, N and S, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>7</sub>-C<sub>24</sub> aralkyl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>1</sub>-C<sub>10</sub> alkenoyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C<sub>6</sub>-C<sub>12</sub> aryl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl, substituted C<sub>7</sub>-C<sub>24</sub> aralkyl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>.

3. (Amended) A method as in claim 1 wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is as defined in claim 1.

6. (Amended) A method of claim 1 wherein B of Formula I is an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and W<sub>n</sub> wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group constituting of halogen and W<sub>n</sub>, whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and W<sub>n</sub> wherein W and n are as defined in claim 1.

7. (Amended) A method of claim 6 wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, -OH, up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy or



phenyl substituted by halogen up to per halo.

8. (Amended) A method of claim 1, wherein L, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and W<sub>n</sub> wherein W and n are as defined in claim 1.

9. (Amended) A method of claim 8, wherein L, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.

10. (Amended) A method of claim 1, wherein said substituted cyclic moiety L<sup>1</sup> comprises a 5 to 6 membered aryl moiety or hetaryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.

11. (Amended) A method of claim 2, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

12. (Amended) A method of claim 3, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

13. (Amended) A method of claim 8, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

15. (Amended) A method of claim 8, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

17. (Amended) A method of claim 10, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

18. (Amended) A method of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m=

1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

19. (Amended) A method of claim 15, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

21. (Amended) A method of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

27. (Amended) A method of claim 21 wherein L<sup>1</sup> is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl, up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, -CN, -OH, halogen, C<sub>1</sub>-C<sub>10</sub> alkoxy and up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy.

28. (Amended) A method of claim 1 wherein L<sup>1</sup> is substituted by -C(O)R<sub>x</sub>.

32. (Amended) A method of claim 1 wherein L<sup>1</sup> is substituted by -C(O)R<sub>x</sub> or -SO<sub>2</sub>R<sub>x</sub>, wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub>.

33. (Amended) A method of claim 13 wherein L<sup>1</sup> is substituted by -C(O)R<sub>x</sub> or -SO<sub>2</sub>R<sub>x</sub>, wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub>, and R<sub>a</sub> and R<sub>b</sub> are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-OSi(R<sub>f</sub>)<sub>3</sub> where R<sub>f</sub> is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R<sub>a</sub> or R<sub>b</sub> is -C(O)-, a C<sub>1</sub>-C<sub>5</sub> divalent alkylene group or a substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C<sub>1</sub>-C<sub>5</sub> divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

37. (Amended) A method of claim 21 wherein L<sup>1</sup> is substituted by -C(O)R<sub>x</sub> or -SO<sub>2</sub>R<sub>x</sub>, wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

38. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:

or a pharmaceutically acceptable salt thereof, wherein

D is  $-\text{NH}-\text{C}(\text{O})-\text{NH}-$ ,

A is a substituted moiety of up to 40 carbon atoms of the formula:  $-\text{L}-(\text{M}-\text{L}^1)_q$ , where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D,  $\text{L}^1$  comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and  $\text{L}^1$  contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein  $\text{L}^1$  is substituted by at least one substituent selected from the group consisting of  $-\text{SO}_2\text{R}_x$ ,  $-\text{C}(\text{O})\text{R}_x$  and  $-\text{C}(\text{NR}_y)\text{R}_z$ ,

$\text{R}_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

$\text{R}_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

$\text{R}_x$  is  $\text{R}_z$  or  $\text{NR}_a\text{R}_b$  where  $\text{R}_a$  and  $\text{R}_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-\text{OSi}(\text{R}_t)_3$  where  $\text{R}_t$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by

halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or  $L^1$  is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and  $W_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-C(O)-R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ ,  $-Q-Ar$ , and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NO_2$ ,  $-NR^7C(O)R^7$ ,  $-NR^7C(O)OR^7$  and halogen up to per-halo; with each  $R^7$  independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is  $-O-$ ,  $-S-$ ,  $-N(R^7)-$ ,  $-(CH_2)_m-$ ,  $-C(O)-$ ,  $-CH(OH)-$ ,  $-(CH_2)_mO-$ ,  $-(CH_2)_mS-$ ,  $-(CH_2)_mN(R^7)-$ ,  $-O(CH_2)_m-CHX^a$ ,  $-CX^a_2-$ ,  $-S-(CH_2)_m-$  and  $-N(R^7)(CH_2)_m-$ , where  $m=1-3$ , and  $X^a$  is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to

per-halo, and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each  $Z$  is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ , and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents are selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-COR^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NO_2$ ,  $-NR^7R^7$ ,  $-NR^7C(O)R^7$ , and  $-NR^7C(O)OR^7$ , with  $R^7$  as defined above; and

wherein  $M$  is one or more bridging groups selected from the group consisting of  $-O-$ ,  $-S-$ ,  $-N(R^7)-$ ,  $-(CH_2)_m-$ ,  $-C(O)-$ ,  $-CH(OH)-$ ,  $-(CH_2)_mO-$ ,  $-(CH_2)_mS-$ ,  $-(CH_2)_mN(R^7)-$ ,  $-O(CH_2)_m-$ ,  $-CHX^a-$ ,  $-CX^a_2-$ ,  $-S-(CH_2)_m-$  and  $-N(R^7)(CH_2)_m-$ , where  $m=1-3$ ,  $X^a$  is halogen.

39. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

$D$  is  $-NH-C(O)-NH-$ ,

$A$  is a substituted moiety of up to 40 carbon atoms of the formula:  $-L-(M-L^1)_q$ , where  $L$  is a substituted or unsubstituted phenyl or pyridinyl moiety bound directly to  $D$ ,  $L^1$  comprises a substituted phenyl, pyridinyl or pyrimidinyl moiety,  $M$  is a bridging group having at least one atom,  $q$  is an integer of from 1-3; and

$B$  is a substituted or unsubstituted phenyl or pyridine group bound directly to  $D$ ,

wherein  $L^1$  is substituted by at least one substituent selected from the group consisting of  $-SO_2R_x$ ,  $-C(O)R_x$  and  $-C(NR_y)R_z$ ,

$R_x$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and ;

$R_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms

selected from N, S and O and are optionally substituted by halogen;

$R_x$  is  $R_z$  or  $NR_aR_b$  where  $R_a$  and  $R_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

$-OSi(R_t)_3$  where  $R_t$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or  $L^1$  is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and  $W_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-C(O)-R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ ,  $-Q-Ar$ , and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from

the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup> and halogen up to per-halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, and X<sup>a</sup> is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen.

44. (Amended) A method as in claim 38 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, CN, OH, halogen, C<sub>1</sub>-C<sub>10</sub> alkoxy and up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy.

45. (Amended) A method as in claim 39 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, CN, OH, halogen, C<sub>1</sub>-C<sub>10</sub> alkoxy and up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy.

46. (Amended) A method of claim 38 wherein L<sup>1</sup> is substituted by C(O)R<sub>x</sub> or SO<sub>2</sub>R<sub>x</sub>.

47. (Amended) A method of claim 39 wherein L<sup>1</sup> is substituted by C(O)R<sub>x</sub> or SO<sub>2</sub>R<sub>x</sub>.





maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

53. (Amended) A method of claim 38 wherein the compound formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

54. (Amended) A method of claim 39 wherein the compound of formula 1 is a pharmaceutically acceptable salt selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

Please add new claims 68-83 as follows.

--68. A method as in claim 1 for the treatment of solid cancers.

69. A method as in claim 1 for the treatment of carcinomas, myleoid disorders or adenomas.

70. A method as in claim 28 for the treatment of carcinomas, myleoid disorders or adenomas.

71. A method as in claim 39 for the treatment of carcinomas, myleoid disorders or adenomas.

72. A method as in claim 50 for the treatment of carcinomas, myleoid disorders or adenomas.

73. A method as in claim 67 for the treatment of carcinomas, myleoid disorders or adenomas.

74. A method as in claim 1 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

75. A method as in claim 28 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

76. A method as in claim 39 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

77. A method as in claim 50 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

78. A method as in claim 67 for the treatment of carcinoma of the lung, pancreas, thyroid, bladder or colon.

79. A method as in claim 1 for the treatment of myeloid leukemia or villous colon adenomas.

80. A method as in claim 28 for the treatment of myeloid leukemia or villous colon adenomas.

81. A method as in claim 39 for the treatment of myeloid leukemia or villous colon adenomas.

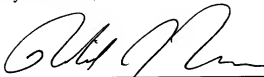
82. A method as in claim 50 for the treatment of myeloid leukemia or villous colon adenomas.

83. A method as in claim 67 for the treatment of myeloid leukemia or villous colon adenomas.--

**REMARKS**

Support for new claims 68-83 is found on page 2, lines 21-24, and page 11, line 9 - page 14, line 30.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**IN THE CLAIMS**

claims 4, 5, 14, 16, 20, 23-26, 29-31, 34-36, 40-43, 51 and 55-65 have been canceled.

Claims 1-3, 6-13, 15, 17-19, 21, 27, 28, 32, 33, 37-39, 44-50 and 52-54 have been amended as follows:

1. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-NH-C(O)-NH-$ ,

A is a substituted moiety of up to 40 carbon atoms of the formula:  $-L-(M-L^1)_q$ , where L is a 5 or 6 membered cyclic structure bound directly to D,  $L^1$  comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and  $L^1$  contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein  $L^1$  is substituted by at least one substituent selected from the group consisting of  $-SO_2R_x$ ,  $-C(O)R_x$  and  $-C(NR_y)R_z$ ,

$R_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

$R_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and

carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

$R_x$  is  $R_z$  or  $NR_aR_b$  where  $R_a$  and  $R_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_l)_3$  where  $R_l$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_3$  divalent alkylene group or a substituted  $C_1-C_3$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_3$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or  $L^1$  is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and  $W_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup> and halogen up to per-halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, and X<sup>a</sup> is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>, with R<sup>7</sup> as defined above.

2. (Amended) A method [compound] as in claim 1 wherein:

R<sub>y</sub> is hydrogen, C<sub>1-10</sub> alkyl, C<sub>1-10</sub> alkoxy, C<sub>3-10</sub> cycloalkyl having 0-3 heteroatoms, C<sub>2-10</sub> alkenyl, C<sub>1-10</sub> alkenoyl, C<sub>6-12</sub> aryl, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>7-24</sub> aralkyl, C<sub>7-24</sub> alkaryl, substituted C<sub>1-10</sub> alkyl, substituted C<sub>1-10</sub> alkoxy, substituted C<sub>3-10</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C<sub>6</sub>-C<sub>14</sub> aryl, substituted C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C<sub>7-24</sub> alkaryl or substituted C<sub>7-24</sub> aralkyl, where R<sub>y</sub> is a substituted group, it is substituted by halogen up to per halo,



$R_z$  is hydrogen,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl having 0-3 heteroatom,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkenoyl,  $C_{6-12}$  aryl,  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from S, N and O,  $C_{7-24}$  aralkyl,  $C_{7-24}$  aralkyl, substituted  $C_{1-10}$  alkyl, substituted  $C_{1-10}$  alkoxy, substituted  $C_6-C_{14}$  aryl, substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from S, N and O, substituted  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from S, N and O, substituted  $C_{7-24}$  aralkyl or substituted  $C_7-C_{24}$  aralkyl where  $R_z$  is a substituted group, it is substituted by halogen up to per halo, hydroxy,  $C_{1-10}$  alkyl,  $C_{3-12}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O,  $C_{1-10}$  alkoxy,  $C_{6-12}$  aryl,  $C_{1-6}$  halo substituted alkyl up to per halo alkyl,  $C_6-C_{12}$  halo substituted aryl up to per halo aryl,  $C_3-C_{12}$  halo substituted cycloalkyl up to per halo cycloalkyl having 0-3 heteroatoms selected from N, S and O, halo substituted  $C_3-C_{12}$  hetaryl up to per halo hetaryl having 1-3 heteroatoms selected from O, N and S, halo substituted  $C_7-C_{24}$  aralkyl up to per halo aralkyl, halo substituted  $C_7-C_{24}$  alkaryl up to per halo alkaryl, and  $-C(O)R_g$ ,

$R_a$  and  $R_b$  are,

a) independently hydrogen,

a carbon based moiety selected from the group consisting of  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_{3-10}$  cycloalkyl,  $C_{2-10}$  alkenyl,  $C_{1-10}$  alkenoyl,  $C_{6-12}$  aryl,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from O, N and S,  $C_{3-12}$  cycloalkyl having 0-3 heteroatoms selected from N, S and O,  $C_{7-24}$  aralkyl,  $C_7-C_{24}$  alkaryl, substituted  $C_{1-10}$  alkyl, substituted  $C_{1-10}$  alkoxy, substituted  $C_{3-10}$  cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted  $C_{6-12}$  aryl, substituted  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O, substituted  $C_{7-24}$  aralkyl, substituted  $C_{7-24}$  alkaryl, where  $R_a$  and  $R_b$  are a substituted group, they are substituted by halogen up to per halo, hydroxy,  $C_{1-10}$  alkyl,  $C_{3-12}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O,  $C_{1-10}$  alkoxy,  $C_{6-12}$  aryl,  $C_{1-6}$  halo substituted alkyl up to per halo alkyl,  $C_6-C_{12}$  halo substituted aryl up to per halo aryl,  $C_3-C_{12}$  halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted  $C_3-C_{12}$  hetaryl up to per halo heteraryl, halo substituted  $C_7-$

C<sub>24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7</sub>-C<sub>24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>; or

-OSi(R<sub>i</sub>)<sub>3</sub> where R<sub>i</sub> is hydrogen, C<sub>1-10</sub> alkyl, C<sub>1-10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>6-12</sub> aryl, C<sub>3</sub>-C<sub>12</sub> hetaryl having 1-3 heteroatoms selected from O, S and N, C<sub>7-24</sub> aralkyl, substituted C<sub>1-10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, substituted C<sub>3</sub>-C<sub>12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, substituted C<sub>3</sub>-C<sub>12</sub> heteraryl having 1-3 heteroatoms selected from O, S, and N, substituted C<sub>6-12</sub> aryl, and substituted C<sub>7-24</sub> alkaryl, where R<sub>i</sub> is a substituted group it is substituted halogen up to per halo, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>7</sub>-C<sub>24</sub> aralkyl, C<sub>1-6</sub> halo substituted alkyl up to per halo alkyl, C<sub>6</sub>-C<sub>12</sub> halo substituted aryl up to per halo aryl, C<sub>3</sub>-C<sub>12</sub> halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7</sub>-C<sub>24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7</sub>-C<sub>24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

or

b) R<sub>a</sub> and R<sub>b</sub> together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O with substituents selected from the group consisting of halogen up to per halo, hydroxy, C<sub>1-10</sub> alkyl, C<sub>3-12</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>3-12</sub> hetaryl having 1-3 heteroatoms selected from N, S and O, C<sub>1-10</sub> alkoxy, C<sub>6-12</sub> aryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>7</sub>-C<sub>24</sub> aralkyl, halo substituted C<sub>1-6</sub> alkyl up to per halo alkyl, halo substituted C<sub>6</sub>-C<sub>12</sub> aryl up to per halo aryl, halo substituted C<sub>3</sub>-C<sub>12</sub> cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C<sub>3</sub>-C<sub>12</sub> hetaryl up to per halo heteraryl, halo substituted C<sub>7</sub>-C<sub>24</sub> aralkyl up to per halo aralkyl, halo substituted C<sub>7</sub>-C<sub>24</sub> alkaryl up to per halo alkaryl, and -C(O)R<sub>g</sub>,

or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy,  $C_{1-10}$  alkyl,  $C_{3-12}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_{3-12}$  hetaryl having 1-3 heteroatoms selected from N, S and O,  $C_{1-10}$  alkoxy,  $C_{6-12}$  aryl,  $C_7-C_{24}$  alkaryl,  $C_7-C_{24}$  aralkyl,  $C_{1-6}$  halo substituted alkyl up to per halo alkyl,  $C_6-C_{12}$  halo substituted aryl up to per halo aryl,  $C_3-C_{12}$  halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted  $C_3-C_{12}$  hetaryl up to per halo heteraryl, halo substituted  $C_7-C_{24}$  alkaryl up to per halo alkaryl, halo substituted  $C_7-C_{24}$  alkaryl up to per halo alkaryl, and  $-C(O)R_g$ ,

where  $R_g$  is  $C_{1-10}$  alkyl;  $-CN$ ,  $-CO_2R_d$ ,  $-OR_d$ ,  $-SR_d$ ,  $-NO_2$ ,  $-C(O)R_e$ ,  $-NR_dR_e$ ,  $-NR_dC(O)OR_e$  and  $-NR_dC(O)R_e$ , and  $R_d$  and  $R_e$  are independently selected from the group consisting of hydrogen,  $C_{1-10}$  alkyl,  $C_{1-10}$  alkoxy,  $C_{3-10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S,  $C_{6-12}$  aryl,  $C_3-C_{12}$  hetaryl with 1-3 heteroatoms selected from O, N and S and  $C_7-C_{24}$  aralkyl,  $C_7-C_{24}$  alkaryl, up to per halo substituted  $C_1-C_{10}$  alkyl, up to per halo substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted  $C_6-C_{14}$  aryl, up to per halo substituted  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted  $C_7-C_{24}$  alkaryl up to per halo alkaryl, and up to per halo substituted  $C_7-C_{24}$  aralkyl,

W is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-C(O)-R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ ,  $C_1-C_{10}$  alkyl,  $C_1-C_{10}$  alkoxy,  $C_2-C_{10}$  alkenyl,  $C_1-C_{10}$  alkenoyl,  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, S and N,  $C_6-C_{14}$  aryl,  $C_7-C_{24}$  alkaryl,  $C_7-C_{24}$  aralkyl,  $C_3-C_{12}$  heteroaryl having 1-3 heteroatoms selected from O, N and S,  $C_4-C_{23}$  alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted  $C_1-C_{10}$  alkyl, substituted  $C_1-C_{10}$  alkoxy, substituted  $C_2-C_{10}$  alkenyl, substituted  $C_1-C_{10}$  alkenoyl, substituted  $C_3-C_{10}$  cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted  $C_6-C_{12}$  aryl, substituted  $C_3-C_{12}$  hetaryl having 1-3 heteroatoms selected from O, N and

S, substituted C<sub>7</sub>-C<sub>24</sub> aralkyl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl, substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and -Q-Ar;

R<sup>7</sup> is independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkenoyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, S and N, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> hetaryl having 1-3 heteroatoms selected from O, N and S, C<sub>7</sub>-C<sub>14</sub> alkaryl, C<sub>7</sub>-C<sub>24</sub> aralkyl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per-halosubstituted C<sub>6</sub>-C<sub>14</sub> aryl, up to per-halosubstituted C<sub>3</sub>-C<sub>13</sub> hetaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C<sub>7</sub>-C<sub>24</sub> aralkyl, up to per-halosubstituted C<sub>7</sub>-C<sub>24</sub> alkaryl, and up to per-halosubstituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl; and

each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>2</sub>-C<sub>10</sub> alkenyl, C<sub>1</sub>-C<sub>10</sub> alkenoyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, N and S, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> hetaryl having 1-3 heteroatoms selected from O, N and S, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>7</sub>-C<sub>24</sub> aralkyl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>1</sub>-C<sub>10</sub> alkoxy, substituted C<sub>2</sub>-C<sub>10</sub> alkenyl, substituted C<sub>1</sub>-C<sub>10</sub> alkenoyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C<sub>6</sub>-C<sub>12</sub> aryl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl, substituted C<sub>7</sub>-C<sub>24</sub> aralkyl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>.

3. (Amended) A method [compound] as in claim 1 wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>x</sup>-, -CX<sup>x</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>x</sup> is halogen and R<sup>7</sup> is as defined in claim 1.

6. (Amended) A method [compound] of claim 1 wherein B of Formula I is an unsubstituted phenyl group, an unsubstituted pyridyl group, an unsubstituted pyrimidinyl, a phenyl group substituted by a substituent selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1, a pyrimidinyl group substituted by a substituent selected from the group constituting of halogen and Wn, whereas W and n are as defined in Claim 1, or a substituted pyridyl group substituted by a substituent selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1.

7. (Amended) A method [compound] of claim 6 wherein B of Formula I is a substituted phenyl group, a substituted pyrimidinyl group, or substituted pyridyl group substituted 1 to 3 times by 1 or more substituents selected from the group consisting of -CN, halogen, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, -OH, up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy or phenyl substituted by halogen up to per halo.

8. (Amended) A method [compound] of claim 1, wherein L, the six member cyclic structure bound directly to D, is a substituted or unsubstituted 6 member aryl moiety or a substituted or unsubstituted 6 member hetaryl moiety, wherein said hetaryl moiety has 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur with the balance of said hetaryl moiety being carbon, wherein the one or more substituents are selected from the group consisting of halogen and Wn wherein W and n are as defined in claim 1.

9. (Amended) A method [compound] of claim 8, wherein L, the 6 member cyclic structure bound directly to D, is a substituted phenyl, unsubstituted phenyl, substituted pyrimidinyl, unsubstituted pyrimidinyl, substituted pyridyl or unsubstituted pyridyl group.

10. (Amended) A method [compound] of claim 1, wherein said substituted cyclic moiety L<sup>1</sup> comprises a 5 to 6 membered aryl moiety or hetaryl moiety, wherein said heteraryl moiety comprises 1 to 4 members selected from the group of heteroatoms consisting of nitrogen, oxygen and sulfur.

11. (Amended) A method [compound] of claim 2, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

12. (Amended) A method [compound] of claim 3, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

13. (Amended) A method [compound] of claim 8, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

15. (Amended) A method [compound] of claim 8, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

17. (Amended) A method [compound] of claim 10, wherein said substituted cyclic moiety L<sup>1</sup> is phenyl, pyridinyl or pyrimidinyl.

18. (Amended) A method [compound] of claim 17 [12], wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

19. (Amended) A method [compound] of claim 15, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

21. (Amended) A method [compound] of claim 17, wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen and R<sup>7</sup> is hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen up to per halo.

27. (Amended) A method [compound] of claim 21 wherein  $L^1$  is additionally substituted 1 to 3 times by one or more substituents selected from the group consisting of  $C_1$ - $C_{10}$  alkyl, up to per halo substituted  $C_1$ - $C_{10}$  alkyl, -CN, -OH, halogen,  $C_1$ - $C_{10}$  alkoxy and up to per halo substituted  $C_1$ - $C_{10}$  alkoxy.

28. (Amended) A method [compound] of claim 1 wherein  $L^1$  is substituted by - $C(O)R_x$ .

32. (Amended) A method [compound] of claim 1 wherein  $L^1$  is substituted by - $C(O)R_x$  or  $-SO_2R_x$ , wherein  $R_x$  is  $NR_aR_b$ .

33. (Amended) A method [compound] of claim 13 wherein  $L^1$  is substituted by - $C(O)R_x$  or  $-SO_2R_x$ , wherein  $R_x$  is  $NR_aR_b$ , and  $R_a$  and  $R_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$  where  $R_f$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

37. (Amended) A method [compound] of claim 21 wherein  $L^1$  is substituted by  $-C(O)R_x$  or  $-SO_2R_x$ , wherein  $R_x$  is  $NR_aR_b$  and  $R_a$  and  $R_b$  are independently hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

38. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-NH-C(O)-NH-$ ,

A is a substituted moiety of up to 40 carbon atoms of the formula:  $-L-(M-L^1)_q$ , where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D,  $L^1$  comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and  $L^1$  contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

wherein  $L^1$  is substituted by at least one substituent selected from the group consisting of  $-SO_2R_x$ ,  $-C(O)R_x$  and  $-C(NR_y)R_z$ ,



$R_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo,

$R_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

$R_x$  is  $R_z$  or  $NR_aR_b$  where  $R_a$  and  $R_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_t)_3$  where  $R_t$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $R_a$  and  $R_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L<sup>1</sup> is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W<sub>n</sub>, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -C(O)-R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>C(O)R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup> and halogen up to per-halo; with each R<sup>7</sup> independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, and X<sup>a</sup> is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -C(O)R<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -NO<sub>2</sub>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)OR<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents are selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>, with R<sup>7</sup> as defined above; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>- CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen.

39. (Amended) A method for the treatment of cancerous cell growth mediated by RAF kinase, comprising administering a compound of Formula I:



or a pharmaceutically acceptable salt thereof, wherein

D is  $-\text{NH}-\text{C}(\text{O})-\text{NH}-$ ,

A is a substituted moiety of up to 40 carbon atoms of the formula:  $-\text{L}-(\text{M}-\text{L}^1)_q$ , where L is a substituted or unsubstituted phenyl or [peritoneal] pyridinyl moiety bound directly to D,  $\text{L}^1$  comprises a substituted phenyl, [peritoneal] pyridinyl or [pyrimidinyl] pyrimidinyl moiety, M is a bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted phenyl or pyridine group bound directly to D,

wherein  $\text{L}^1$  is substituted by at least one substituent selected from the group consisting of  $-\text{SO}_2\text{R}_x$ ,  $-\text{C}(\text{O})\text{R}_x$  and  $-\text{C}(\text{NR}_y)\text{R}_z$ ,

$\text{R}_y$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo, and ;

$\text{R}_z$  is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

$\text{R}_x$  is  $\text{R}_z$  or  $\text{NR}_a\text{R}_b$  where  $\text{R}_a$  and  $\text{R}_b$  are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-\text{OSi}(\text{R}_t)_3$  where  $\text{R}_t$  is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b)  $\text{R}_a$  and  $\text{R}_b$  together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms

selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of  $R_a$  or  $R_b$  is  $-C(O)-$ , a  $C_1-C_5$  divalent alkylene group or a substituted  $C_1-C_5$  divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted  $C_1-C_5$  divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or  $L^1$  is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and  $W_n$ , where n is 0-3;

wherein each W is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)NR^7R^7$ ,  $-C(O)-R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ ,  $-Q-Ar$ , and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NO_2$ ,  $-NR^7C(O)R^7$ ,  $-NR^7C(O)OR^7$  and halogen up to per-halo; with each  $R^7$  independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is  $-O-$ ,  $-S-$ ,  $-N(R^7)-$ ,  $-(CH_2)_m-$ ,  $-C(O)-$ ,  $-CH(OH)-$ ,  $-(CH_2)_mO-$ ,  $-(CH_2)_mS-$ ,  $-(CH_2)_mN(R^7)-$ ,  $-O(CH_2)_m-CHX^a$ ,  $-CX^a_2-$ ,  $-S-(CH_2)_m-$  and  $-N(R^7)(CH_2)_m-$ , where  $m=1-3$ , and  $X^a$  is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by  $Z_{n1}$ , wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^7$ ,  $-C(O)R^7$ ,  $-C(O)NR^7R^7$ ,  $-NO_2$ ,  $-OR^7$ ,  $-SR^7$ ,  $-NR^7R^7$ ,  $-NR^7C(O)OR^7$ ,  $-NR^7C(O)R^7$ , and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one

or more substituents selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>7</sup>, -COR<sup>7</sup>, -C(O)NR<sup>7</sup>R<sup>7</sup>, -OR<sup>7</sup>, -SR<sup>7</sup>, -NO<sub>2</sub>, -NR<sup>7</sup>R<sup>7</sup>, -NR<sup>7</sup>C(O)R<sup>7</sup>, and -NR<sup>7</sup>C(O)OR<sup>7</sup>; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -N(R<sup>7</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>7</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-CHX<sup>a</sup>-, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>7</sup>)(CH<sub>2</sub>)<sub>m</sub>-, where m= 1-3, X<sup>a</sup> is halogen.

44. (Amended) A method [compound] as in claim 38 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, CN, OH, halogen, C<sub>1</sub>-C<sub>10</sub> alkoxy and up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy.

45. (Amended) A method [compound] as in claim 39 wherein substituents for B and L and additional substituents for L<sup>1</sup>, are selected from the group consisting of C<sub>1</sub>-C<sub>10</sub> alkyl up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkyl, CN, OH, halogen, C<sub>1</sub>-C<sub>10</sub> alkoxy and up to per halo substituted C<sub>1</sub>-C<sub>10</sub> alkoxy.

46. (Amended) A method [compound] of claim 38 wherein L<sup>1</sup> is substituted by C(O)R<sub>x</sub> or SO<sub>2</sub>R<sub>x</sub>.

47. (Amended) A method [compound] of claim 39 wherein L<sup>1</sup> is substituted by C(O)R<sub>x</sub> or SO<sub>2</sub>R<sub>x</sub>.

48. (Amended) A method [compound] of claim 46 wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen..

49. (Amended) A method [compound] of claim 47 wherein R<sub>x</sub> is NR<sub>a</sub>R<sub>b</sub> and R<sub>a</sub> and R<sub>b</sub> are independently hydrogen and a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

50. (Amended) A method [compound] of claim 1 wherein the compound of formula 1 [which] is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

52. (Amended) A method [compound] of claim 33 wherein the compound of formula 1 [which] is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

53. (Amended) A method [compound] of claim 38 [which] wherein the compound of formula 1 is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.

54. (Amended) A method [compound] of claim 39 [which] wherein the compound of formula 1 is a pharmaceutically acceptable salt [of a compound of formula I] selected from the group consisting of

a) basic salts of organic acids and inorganic acids selected from the group consisting of hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulphonic acid, trifluorosulphonic acid, benzenesulfonic acid, p-toluene sulphonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, and mandelic acid; and

b) acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations.